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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,751	04/02/2004	Shotaro Yamaguchi	Q80536	1552

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SUGHRUE MION, PLLC
2100 Pennsylvania Avenue, NW
Washington, DC 20037-3213

EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/815,751	YAMAGUCHI ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/324,910.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

New Claims 25-34 are currently pending in this application. Original claims 1-24 have been cancelled by the applicants in the preliminary amendment filed on 4-2-04.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 4-2-04 has been considered by the examiner.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Specification

Examiner notes that applicants have not updated the relationship of the instant application to its parent application that has matured in to a US patent. Examiner urges applicants to amend said information by providing the US patent number in response to this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 26-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 26-28 recite the phrase "such that the functionality of said protein or

peptide/food/extraction efficiency is improved". The metes and bounds of this phrase specifically of the terms "functionality" and "improved" is not clear to the Examiner. It is not clear as to how one skilled in the art would identify as to what functionalities are encompassed and how one skilled in the art would conclude that such a functionality is improved and in comparison to which peptide or polypeptide.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for modifying a target protein or peptide with a molecular weight of 5,000 or more, comprising allowing the polypeptide with SEQ ID NO:6 and encoded by the polynucleotide SEQID NO:5 wherein the polypeptide is an enzyme, which is capable of deamidating amido groups in target proteins and peptides by directly acting upon said amido groups without cutting peptide bonds and without cross-linking said target proteins or peptides, does not reasonably provide enablement for such a method comprising modifying a target protein or peptide with any molecular weight and allowing any or all enzymes capable of deamidating amido groups in target proteins and peptides by directly acting upon said amido groups without cutting peptide bonds and without cross-linking said target proteins or peptides, including mutants and variants of SEQ ID NO:6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 25-34 are so broad as to encompass any deamidating enzyme including variants, mutants and recombinants of SEQ ID NO:6. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of enzymes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only single specific deamidase with SEQ ID NO:6. It would require undue experimentation of the skilled artisan to make and use the polypeptides in the claimed method. The specification is limited to teaching the use of SEQ ID NO: 6 the specific enzyme that can be used in the claimed method but provides no guidance with regard to the making of variants and mutants of SEQ ID NO:6 or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the polypeptides for use in the claimed method, the lack of guidance, working

examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompasses method of using any or all deamidating enzymes including polypeptides comprising all modifications and fragments of SEQ ID NOS:6 because the specification does not establish: (A) regions of the protein structure which may be modified without affecting deamidating activity; (B) the general tolerance of said deamidases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue on the polypeptide SEQ ID NO:6 with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polypeptides with an enormous number of amino acid modifications in SEQ ID NOS: 6. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics for use in the claimed method is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 25-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 25-34 are directed to a method of use of polypeptides and fragments corresponding to the sequence of SEQ ID NO:6 and variants, mutants and recombinants of SEQ ID NO:6. Claims 25-34 are rejected under this section of 35 USC 112 because the claims are directed to a method of use of a genus of polypeptides derived from SEQ ID NO:6 including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue in SEQ ID NO:6 and fragments of SEQ ID NO:6 that have not been disclosed in the specification. No description has been provided of the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization

of SEQ ID NO:6 has been provided by applicants, which would indicate that they had possession of the genus of modified polypeptides for use in the claimed method. The specification does not contain any disclosure of the structure of all the polypeptide sequences derived from SEQ ID NO:6, including fragments and variants within the scope of the genus of polypeptides to be used in the claimed method. The genus of polypeptides required for the claimed method is a large variable genus including peptides, which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 25-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Vaintraub et al. (FEBS Lett. 1992, Vol. 302(2):169-171). This rejection is based upon the public availability of a

printed publication. Claims 25-28 of the instant application are drawn to a method of modifying a target protein or peptide, comprising allowing an enzyme, which is capable of deamidating amido groups in target proteins and peptides by directly acting upon said amido groups without cutting peptide bonds and without cross-linking said target proteins or peptides, to act on said target protein or peptide wherein said target protein or peptide to be modified is derived from a plant or animal such that the functionality of said protein or peptide is improved and wherein said target protein or peptide to be modified is derived from food such that the functionality of said food is improved and wherein said target protein or peptide is contained in a crude material such that the extraction efficiency of said target protein or peptide is improved.

Vaintraub et al. teach such a method of modifying a target protein such as wheat protein comprising allowing a deamidase to deamidate the amido groups without hydrolyzing the target protein wherein said target protein is derived from a plan or a food and wherein the functionality of said target protein is improved. Examiner is aware that the reference does not specifically disclose that said enzyme is capable of deamidating amido groups in target proteins and peptides by directly acting upon said amido groups without cutting peptide bonds and without cross-linking said target proteins or peptides. However, it must be recognized that the reference does not specifically disclose that said enzyme does not have the above characteristic. In view of the above reasoning Examiner takes the stand that the reference enzyme and the enzyme used in the above claimed method are one and the same and therefore Vaintraub et al. anticipate claims 25-28.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vaintraub et al. as applied to claims 25-28 above, and further in view of Hamada et al. (US5,082,672, issued Jan 21, 1992 and Gottmann et al. (US 5,279,839 issued Jan 18, 1994). Claims 29-34 are drawn to method of modifying a target protein or peptide, comprising allowing an enzyme, which is capable of deamidating amido groups in target proteins and peptides, wherein said method further comprises the step of allowing transglutaminase to act on said target protein. The method also comprises the step of reacting the target protein with the transglutaminase either before or after contact with a deamidase.

The reference of Vaintraub et al., which teaches the method of modifying a target food protein with a deamidase leading to improvement of the target protein, has already been discussed above. However, the reference of Vaintraub et al. does not specifically teach a method of reacting the target protein with a transglutaminase either before or after the reaction with a deamidase.

The references of Hamada et al. and Gottmann et al. teach the advantages of reacting a food protein or food comprising largely of proteins to a transglutaminase. The reference specifically teach that doing so improves the quality of the baked products comprising said treated proteins.

Combining the teachings of the above references it would have been obvious to one of ordinary skill in the art to deamidate the wheat protein in wheat flour first with a deamidase followed by a treatment with transglutaminase or vice versa, such that a bakery product prepared with such treated wheat flour would have improved baked qualities. One of ordinary skill in the art would have been motivated to do so in view of the teachings in all the references the advantages of such a treatment. One of ordinary skill in the art would have a reasonable expectation of success since the reference of Vaintraub et al. provides the source of said deamidase in addition to teaching the advantages of treating wheat flour with said enzyme and the references of Gottmann and Hamada teach the advantages of treating wheat flour with transglutaminase.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and

useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

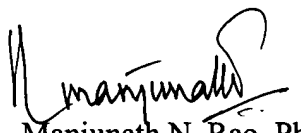
Claims 25-27 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-12 of prior U.S. Patent No. 6,756,221. This is a double patenting rejection.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652
September 29, 2006